

81010

STIC-Biotech/ChemLib

From: Rao, Manjunath N.
Sent: Monday, November 25, 2002 9:20 AM
To: STIC-Biotech/ChemLib
Subject: Sequence search request for 09/806,088

RECEIVED

NOV 25 2002

(STIC)

From: Manjunath N. Rao
Art Unit 1652, Room 10A11
Mail Box in Room 10D 01
Phone: 306-5681

Date: 11-25-02

Please search the following as soon as possible for application with serial number **09/806,088**

SEQ ID NO: 1, against a specific reference sequence with **Accession No. AF139813** in GenEmbl Database. Examiner is aware that SEQ ID NO:1 is a jumbo sequence. He has found a match in a segment search done previously and now wants to confirm that the reference is a 100% match.

If you have any questions please call me at the above phone number.

Thanks
Manjunath

A.U. 1652

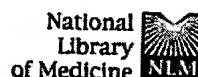
Manjunath N. Rao, Ph.D.
Biotechnology Patent Examiner
Art Unit 1652, Room 10A11
Crystal Mall 1, USPTO.

POINT OF CONTACT:
PAUL SCHULWITZ
TECHNICAL INFO. SPECIALIST
CM1 6B06 TEL. (703) 305-1954

Searcher: _____
Phone: _____
Location: _____
Date Picked Up: 11/29
Date Completed: 12/3
Searcher Prep/Review: SO
Clerical: _____
Online time: 10

TYPE OF SEARCH:
NA Sequences: _____
AA Sequences: _____
Structures: _____
Bibliographic: _____
Litigation: _____
Full text: _____
Patent Family: _____
Other: _____

VENDOR/COST (where applic.)
STN: _____
DIALOG: _____
Questel/Orbit: _____
DRLink: _____
Lexis/Nexis: _____
Sequence Sys.: _____
WWW/Internet: _____
Other (specify): _____



PubMed	Nucleotide	Protein	Genome	Structure	PMC	Taxonomy	OMIM	Books	
Search PubMed	▼ for							Go	Clear
<input checked="" type="checkbox"/> Limits		Preview/Index	History	Clipboard	Details				
Display	Abstract	▼ Show: 20		▼ Sort		▼ Send to: Text		▼	

Entrez
PubMed☐ 1: Eur J Biochem 1995 Sep 15;232(3):798-805[Related Articles, Links](#)

A cytochrome-b5-containing fusion protein similar to plant acyl lipid desaturases.

Sperling P, Schmidt H, Heinz E.

PubMed
Services

Institut für Allgemeine Botanik, Universität Hamburg, Germany.

Related
Resources

The similarity between oleate and linoleate desaturase sequences from several plants was used to construct degenerate oligonucleotide primers for PCR experiments with cDNA transcribed from mRNA of ripening sunflower embryos. A DNA fragment was amplified and sequenced. Specific primers derived from this partial sequence were used for rapid amplification of the 3'- and 5'-ends of this cDNA. With appropriate primers derived from these sequences, a full-length clone of 1377 bp was amplified by PCR which, after sequencing, showed an open reading frame of 458 amino acids corresponding to a putative protein of about 52 kDa. Comparison with other desaturases showed the conserved three histidine boxes and the characteristic hydrophathy profile of membrane-bound desaturases, but the amino acid identity was restricted to 18% and the N-terminal region was about 100 amino acids longer. This N-terminal extension showed high similarity with cytochrome b5 and, accordingly, the whole sequence can be considered as coding for a fusion protein between cytochrome b5 and a desaturase-like enzyme. Furthermore, we detected a similar cytochrome b5 fold in the previously sequenced delta 9 acyl-CoA desaturase from yeast, but in this enzyme it was located at the C-terminus. An alignment of these fusion proteins with other heme-binding proteins revealed desaturases to be novel members of the cytochrome b5 superfamily. A truncated DNA representing 366 bp of the 5'-end was amplified from the cDNA clone and expressed in *Escherichia coli*. The truncated cDNA coded for a soluble protein of about 12 kDa as shown by SDS/PAGE and N-terminal sequencing. The enriched recombinant protein exhibited redox absorbance spectra characteristic of plant microsomal cytochrome b5.

PMID: 7588718 [PubMed - indexed for MEDLINE]

Display	Abstract	▼ Show: 20		▼ Sort		▼ Send to: Text		▼	
---------	----------	------------	--	--------	--	-----------------	--	---	--

WEST[Help](#)[Logout](#)[Interrupt](#)[Main Menu](#)[Search Form](#)[Posting Counts](#)[Show S Numbers](#)[Edit S Numbers](#)[Preferences](#)[Cases](#)**Search Results -**

Terms	Documents
L2 with (cDNA or clone)	15

Database:

US Patents Full-Text Database
US Pre-Grant Publication Full-Text Database
JPO Abstracts Database
EPO Abstracts Database
Derwent World Patents Index

IBM Technical Disclosure Bulletins

Search:

L3

[Refine Search](#)[Recall Text](#)[Clear](#)**Search History****DATE:** Monday, November 25, 2002 [Printable Copy](#) [Create Case](#)Set Name
side by sideQueryHit Count Set Name
result set*DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ*

<u>L3</u>	L2 with (cDNA or clone)	15	<u>L3</u>
<u>L2</u>	L1 with (delta 6) or (CYB5RP)	125	<u>L2</u>
<u>L1</u>	desaturase	1083	<u>L1</u>

END OF SEARCH HISTORY

WEST[Generate Collection](#)[Print](#)**Search Results - Record(s) 1 through 15 of 15 returned.**☐ 1. Document ID: US 20020150581 A1

L3: Entry 1 of 15

File: PGPB

Oct 17, 2002

PGPUB-DOCUMENT-NUMBER: 20020150581

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020150581 A1

TITLE: Compositions and methods for the therapy and diagnosis of breast cancer

PUBLICATION-DATE: October 17, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Jiang, Yuqiu	Kent	WA	US	
Dillon, Davin C.	Issaquah	WA	US	
Mitcham, Jennifer L.	Redmond	WA	US	
Xu, Jiangchun	Bellevue	WA	US	
Harlocker, Susan L.	Seattle	WA	US	
Hepler, William T.	Seattle	WA	US	
Henderson, Robert A.	Edmonds	WA	US	
Fanger, Gary R.	Mill Creek	WA	US	
Vedvick, Thomas S.	Federal Way	WA	US	
McNeill, Patricia D.	Federal Way	WA	US	
Durham, Margarita	Seattle	WA	US	

US-CL-CURRENT: 424/155.1; 435/183, 435/320.1, 435/325, 435/6, 435/69.1, 435/7.23, 536/23.2

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	NIMC	Dram Desc	Image
------	-------	----------	-------	--------	----------------	------	-----------	-----------	-------------	--------	------	-----------	-------

☐ 2. Document ID: US 20020108147 A1

L3: Entry 2 of 15

File: PGPB

Aug 8, 2002

PGPUB-DOCUMENT-NUMBER: 20020108147

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020108147 A1

TITLE: Production of gamma linolenic acid by a delta6-desaturase

PUBLICATION-DATE: August 8, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Thomas, Terry L.	College Station	TX	US	

US-CL-CURRENT: 800/281; 536/23.6, 800/278, 800/287

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	RWMC	Draw Desc	Image
------	-------	----------	-------	--------	----------------	------	-----------	-----------	-------------	--------	------	-----------	-------

☐ 3. Document ID: US 20020102602 A1

L3: Entry 3 of 15

File: PGPB

Aug 1, 2002

PGPUB-DOCUMENT-NUMBER: 20020102602

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020102602 A1

TITLE: COMPOSITIONS FOR THE TREATMENT AND DIAGNOSIS OF BREAST CANCER AND METHODS FOR THEIR USE

PUBLICATION-DATE: August 1, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
YUQIU, JIANG	KENT	WA	US	
DILLON, DAVIN C.	SEATTLE	WA	US	
MITCHAM, JENNIFER L.	REDMOND	WA	US	
XU, JIANGCHUN	BELLEVUE	WA	US	

US-CL-CURRENT: 435/7.1; 435/6, 514/2, 514/44

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	RWMC	Draw Desc	Image
------	-------	----------	-------	--------	----------------	------	-----------	-----------	-------------	--------	------	-----------	-------

☐ 4. Document ID: US 20020085998 A1

L3: Entry 4 of 15

File: PGPB

Jul 4, 2002

PGPUB-DOCUMENT-NUMBER: 20020085998

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020085998 A1

TITLE: Compositions and methods for the therapy and diagnosis of breast cancer

PUBLICATION-DATE: July 4, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Jiang, Yuqiu	Kent	WA	US	
Dillon, Davin C.	Issaquah	WA	US	
Mitcham, Jennifer L.	Redmond	WA	US	
Xu, Jiangchun	Bellevue	WA	US	
Harlocker, Susan L.	Seattle	WA	US	
Hepler, William T.	Seattle	WA	US	
Henderson, Robert A.	Edmonds	WA	US	

US-CL-CURRENT: 424/93.21; 435/183, 435/320.1, 435/325, 435/69.1, 536/23.1

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
------	-------	----------	-------	--------	----------------	------	-----------	-----------	-------------

RWMC	Draw Desc	Image
------	-----------	-------

☐ 5. Document ID: US 20020064872 A1

L3: Entry 5 of 15

File: PGPB

May 30, 2002

PGPUB-DOCUMENT-NUMBER: 20020064872
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020064872 A1

TITLE: Compositions and methods for the therapy and diagnosis of breast cancer

PUBLICATION-DATE: May 30, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Jiang, Yuqui	Kent	WA	US	
Dillon, Davin C.	Isaaquah	WA	US	
Mitcham, Jennifer L.	Redmond	WA	US	
Xu, Jiangchun	Bellevue	WA	US	
Harlocker, Susan L.	Seattle	WA	US	
Hepler, William T.	Seattle	WA	US	

US-CL-CURRENT: 435/325; 424/130.1, 424/93.1, 435/7.1, 514/2, 514/44, 530/350,
536/23.1

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
------	-------	----------	-------	--------	----------------	------	-----------	-----------	-------------

KIMC	Draw Desc	Image
------	-----------	-------

☐ 6. Document ID: US 6410288 B1

L3: Entry 6 of 15

File: USPT

Jun 25, 2002

US-PAT-NO: 6410288
DOCUMENT-IDENTIFIER: US 6410288 B1

TITLE: Methods and compositions for synthesis of long chain poly-unsaturated fatty acids

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
------	-------	----------	-------	--------	----------------	------	-----------	-----------	-------------

KIMC	Draw Desc	Image
------	-----------	-------

☐ 7. Document ID: US 6355861 B1

L3: Entry 7 of 15

File: USPT

Mar 12, 2002

US-PAT-NO: 6355861
DOCUMENT-IDENTIFIER: US 6355861 B1

TITLE: Production of gamma linolenic acid by a .DELTA.6-desaturase

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
------	-------	----------	-------	--------	----------------	------	-----------	-----------	-------------

KIMC	Draw Desc	Image
------	-----------	-------

☐ 8. Document ID: US 6136574 A

L3: Entry 8 of 15

File: USPT

Oct 24, 2000

US-PAT-NO: 6136574
DOCUMENT-IDENTIFIER: US 6136574 A

TITLE: Methods and compositions for synthesis of long chain polyunsaturated fatty

acids

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
------	-------	----------	-------	--------	----------------	------	-----------	-----------	-------------

KMNC	Draw Desc	Image
------	-----------	-------

☐ 9. Document ID: US 5977436 A

L3: Entry 9 of 15

File: USPT

Nov 2, 1999

US-PAT-NO: 5977436

DOCUMENT-IDENTIFIER: US 5977436 A

TITLE: Oleosin 5' regulatory region for the modification of plant seed lipid composition

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
------	-------	----------	-------	--------	----------------	------	-----------	-----------	-------------

KMNC	Draw Desc	Image
------	-----------	-------

☐ 10. Document ID: US 5968809 A

L3: Entry 10 of 15

File: USPT

Oct 19, 1999

US-PAT-NO: 5968809

DOCUMENT-IDENTIFIER: US 5968809 A

TITLE: Methods and compositions for synthesis of long chain poly-unsaturated fatty acids

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
------	-------	----------	-------	--------	----------------	------	-----------	-----------	-------------

KMNC	Draw Desc	Image
------	-----------	-------

☐ 11. Document ID: US 5959175 A

L3: Entry 11 of 15

File: USPT

Sep 28, 1999

US-PAT-NO: 5959175

DOCUMENT-IDENTIFIER: US 5959175 A

TITLE: Sunflower albumin 5' regulatory region for the modification of plant seed lipid composition

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
------	-------	----------	-------	--------	----------------	------	-----------	-----------	-------------

KMNC	Draw Desc	Image
------	-----------	-------

☒ 12. Document ID: US 5789220 A

L3: Entry 12 of 15

File: USPT

Aug 4, 1998

US-PAT-NO: 5789220

DOCUMENT-IDENTIFIER: US 5789220 A

TITLE: Production of .gamma.-linolenic acid by a .DELTA.6-desaturase

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
------	-------	----------	-------	--------	----------------	------	-----------	-----------	-------------

KMNC	Draw Desc	Image
------	-----------	-------

☒ 13. Document ID: US 5614393 A

L3: Entry 13 of 15

File: USPT

Mar 25, 1997

US-PAT-NO: 5614393

DOCUMENT-IDENTIFIER: US 5614393 A

TITLE: Production of .gamma.-linolenic acid by a .DELTA.6-desaturase

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
------	-------	----------	-------	--------	----------------	------	-----------	-----------	-------------

KMNC	Draw Desc	Image
------	-----------	-------

☐ 14. Document ID: WO 9927111 A1

L3: Entry 14 of 15

File: EPAB

Jun 3, 1999

PUB-NO: WO009927111A1

DOCUMENT-IDENTIFIER: WO 9927111 A1

TITLE: DESATURASE GENES AND THEIR USE

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
------	-------	----------	-------	--------	----------------	------	-----------	-----------	-------------

KMNC	Draw Desc	Image
------	-----------	-------

☐ 15. Document ID: WO 200032790 A2 AU 200021631 A

L3: Entry 15 of 15

File: DWPI

Jun 8, 2000

DERWENT-ACC-NO: 2000-412336

DERWENT-WEEK: 200035

COPYRIGHT 2002 DERWENT INFORMATION LTD

TITLE: Polynucleotide encoding delta-6 desaturase enzyme useful for producing transgenic plants and for producing antibodies specific to which is useful for screening cDNA expression libraries

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
------	-------	----------	-------	--------	----------------	------	-----------	-----------	-------------

KMNC	Draw Desc	Image
------	-----------	-------

[Generate Collection](#)[Print](#)

Terms	Documents
L2 with (cDNA or clone)	15

Display Format:

-

[Change Format](#)[Previous Page](#)[Next Page](#)

=> d his

(FILE 'HOME' ENTERED AT 15:35:28 ON 25 NOV 2002)

INDEX 'ADISALERTS, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI, BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, ...' ENTERED AT 15:36:30 ON 25 NOV 2002

SEA DESATURASE

13	FILE ADISALERTS
1	FILE ADISINSIGHT
2	FILE ADISNEWS
777	FILE AGRICOLA
9	FILE ANABSTR
104	FILE AQUASCI
92	FILE BIOBUSINESS
27	FILE BIOCOMMERCE
2861	FILE BIOSIS
259	FILE BIOTECHABS
259	FILE BIOTECHDS
811	FILE BIOTECHNO
1180	FILE CABA
314	FILE CANCERLIT
3238	FILE CAPLUS
68	FILE CEABA-VTB
2	FILE CEN
20	FILE CIN
94	FILE CONFSCI
8	FILE CROPB
89	FILE CROPU
14	FILE DDFB
76	FILE DDFU
3138	FILE DGENE
14	FILE DRUGB
105	FILE DRUGU
1	FILE DRUGUPDATES
23	FILE EMBAL
1541	FILE EMBASE
933	FILE ESBIODBASE
110	FILE FEDRIP
205	FILE FROSTI
209	FILE FSTA
4106	FILE GENBANK
1	FILE HEALSAFE
136	FILE IFIPAT
1415	FILE JICST-EPLUS
4	FILE KOSMET
645	FILE LIFESCI
1	FILE MEDICONF
3415	FILE MEDLINE
10	FILE NIOSHTIC
10	FILE NTIS
16	FILE OCEAN
891	FILE PASCAL
1	FILE PHAR
16	FILE PHIN
60	FILE PROMT
2319	FILE SCISEARCH
894	FILE TOXCENTER
818	FILE USPATFULL
7	FILE USPAT2

13 FILE VETU
201 FILE WPIDS
201 FILE WPINDEX
L1 QUE DESATURASE

FILE 'BIOSIS, CAPLUS, MEDLINE, SCISEARCH, EMBASE, JICST-EPLUS, CABA'
ENTERED AT 15:38:14 ON 25 NOV 2002

L2 2919 S L1 AND (DELTA 6) OR (CYB5RP)
L3 1 S L2 AND CYB5RP
L4 2919 S L1 AND (DELTA 6)
L5 173 S L4 AND (CDNA OR CLONE)
L6 32 S L5 AND PY<1998
L7 14 DUP REM L6 (18 DUPLICATES REMOVED)

=> d 17 ibib ab 1-14

L7 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:182219 CAPLUS

DOCUMENT NUMBER: 136:242927

TITLE: Cloning of **.DELTA.6-desaturase** gene from evening primrose and its use in **.gamma. linolenic acid (GLA)** prodn. in transgenic plants

INVENTOR(S): Thomas, Terry L.

PATENT ASSIGNEE(S): Rhone-Poulenc Agrochimie, Fr.

SOURCE: U.S., 53 pp., Cont.-in-part of U.S. 5,789,220.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6355861	B1	20020312	US 1997-934254	19970919
ZA 9207777	A	19930421	ZA 1992-7777	19921009 <--
US 5552306	A	19960903	US 1994-307382	19940914 <--
US 5789220	A	19980804	US 1997-789936	19970128
US 2002108147	A1	20020808	US 2001-29756	20011221
PRIORITY APPLN. INFO.:			US 1991-774475	B2 19911010
			US 1992-817919	B2 19920108
			US 1992-959952	B1 19921013
			US 1994-307382	A2 19940914
			US 1997-789936	A2 19970128
			US 1994-366779	A1 19941230
			US 1997-934254	A1 19970919

AB Linoleic acid is converted into **.gamma.-linolenic acid** by the enzyme **.DELTA.6-desaturase**. The present invention is directed to isolated nucleic acids comprising the **.DELTA.6-desaturase** gene from evening primrose. More particularly, the isolated nucleic acid comprises the promoter, coding region and termination regions of the **.DELTA.6-desaturase** gene. The present invention provides recombinant vectors expressing **.DELTA.6-desaturase** gene controlled by heterologous regulatory promoter and terminator elements. The nucleic acids and recombinant constructions of the instant invention are useful in the prodn. of GLA in transgenic organisms.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:231335 CAPLUS

DOCUMENT NUMBER: 126:289996

TITLE: Microbial and plant genes for **.DELTA.6-desaturases** and their use in increasing tissue levels of **.gamma.-linolenic acid**

INVENTOR(S): Thomas, Terry L.; Reddy, Avutu S.; Nuccio, Michael; Nunberg, Andrew N.; Freyssinet, Georges L.

PATENT ASSIGNEE(S): Rhone-Poulenc Agrochimie, Fr.

SOURCE: U.S., 30 pp., Cont.-in-part of U.S. 5,552,306.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
------------	------	------	-----------------	------

US 5614393	A	19970325	US 1994-366779	19941230 <--
ZA 9207777	A	19930421	ZA 1992-7777	19921009 <--
US 5552306	A	19960903	US 1994-307382	19940914 <--
US 5663068	A	19970902	US 1995-478727	19950607 <--
US 5689050	A	19971118	US 1995-473508	19950607 <--
CA 2207906	AA	19960711	CA 1995-2207906	19951228 <--
WO 9621022	A2	19960711	WO 1995-IB1167	19951228 <--
WO 9621022	A3	19960912		
W: AU, BR, CA, CN, JP, RO, RU, UA				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9646735	A1	19960724	AU 1996-46735	19951228 <--
AU 707061	B2	19990701		
EP 801680	A2	19971022	EP 1995-944464	19951228 <--
R: DE, ES, FR, GB, GR, IT				
CN 1177379	A	19980325	CN 1995-197728	19951228
BR 9510411	A	19980519	BR 1995-10411	19951228
JP 10511848	T2	19981117	JP 1995-520827	19951228
RU 2181772	C2	20020427	RU 1997-112919	19951228
US 5789220	A	19980804	US 1997-789936	19970128

PRIORITY APPLN. INFO.:

US 1991-774475	B2	19911010
US 1992-817919	B2	19920108
US 1992-959952	B1	19921013
US 1994-307382	A2	19940914
US 1994-366779	A	19941230
WO 1995-IB1167	W	19951228

AB Microbial genes for **.DELTA.6-desaturases** are cloned and characterized for use in the prepn. of transgenic organisms synthesizing high levels of .gamma.-linolenic acid from linoleic acid. Plants expressing a **desaturase** gene and with high tissue levels of .gamma.-linolenic acid are chilling resistant. These plants can also be used to produce oils with altered levels .gamma.-linolenic acid. The *Synechocystis* **.DELTA.6-desaturase** was cloned by expression in a .gamma.-linolenate-deficient *Anabaena*. Expression of the gene in transgenic tobacco and carrot is demonstrated.

L7 ANSWER 3 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
1

ACCESSION NUMBER: 1997:217281 BIOSIS

DOCUMENT NUMBER: PREV199799523785

TITLE: Expression of a borage **desaturase cDNA** containing an N-terminal cytochrome b-5 domain results in the accumulation of high levels of **DELTA-6-desaturated fatty acids** in transgenic tobacco.

AUTHOR(S): Sayanova, Olga; Smith, Mark A.; Lapinskas, Peter; Stobart, A. Keith; Dobson, Gary; Christie, William W.; Shewry, Peter R.; Napier, Johnathan A. (1)

CORPORATE SOURCE: (1) Inst. Arable Crops Res.-Long Ashton Res. Station, Univ. Bristol, Long Ashton, Bristol BS18 9AF UK

SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1997) Vol. 94, No. 8, pp. 4211-4216.

ISSN: 0027-8424.

DOCUMENT TYPE: Article

LANGUAGE: English

AB gamma-Linolenic acid (GLA; C18:3 **DELTA-6,9,12**) is a component of the seed oils of evening primrose (*Oenothera* spp.), borage (*Borago officinalis* L.), and some other plants. It is widely used as a dietary supplement and for treatment of various medical conditions. GLA is synthesized by a **delta-6-fatty acid desaturase** using linoleic acid (C18:2 **DELTA-9,12**) as a substrate. To enable the production of GLA in conventional oilseeds, we have isolated a **cDNA** encoding the **DELTA-6-fatty acid desaturase** from developing seeds of borage and confirmed its function by expression in transgenic tobacco plants. Analysis of leaf

lipids from a transformed plant demonstrated the accumulation of GLA and octadecatetraenoic acid (C18:4 **DELTA-6,9,12,15**) to levels of 13.2% and 9.6% of the total fatty acids, respectively. The borage **DELTA-6-fatty acid desaturase** differs from other **desaturase** enzymes, characterized from higher plants previously, by the presence of an N-terminal domain related to cytochrome b-5.

L7 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:531817 CAPLUS

DOCUMENT NUMBER: 125:160370

TITLE: Borago officinalis **.DELTA.6-desaturase cDNA** sequence, .gamma.-linolenic acid production by transgenic plant, and improved resistance to chilling

INVENTOR(S): Thomas, Terry L.; Reddy, Avutu S.; Nuccio, Michael; Nunberg, Andrew N.; Freyssinet, Georges L.

PATENT ASSIGNEE(S): Rhone-Poulenc Agrochimie, Fr.

SOURCE: PCT Int. Appl., 64 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9621022	A2	19960711	WO 1995-IB1167	19951228 <--
WO 9621022	A3	19960912		
W: AU, BR, CA, CN, JP, RO, RU, UA				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5614393	A	19970325	US 1994-366779	19941230 <--
AU 9646735	A1	19960724	AU 1996-46735	19951228 <--
AU 707061	B2	19990701		
EP 801680	A2	19971022	EP 1995-944464	19951228 <--
R: DE, ES, FR, GB, GR, IT				
BR 9510411	A	19980519	BR 1995-10411	19951228
JP 10511848	T2	19981117	JP 1995-520827	19951228
RU 2181772	C2	20020427	RU 1997-112919	19951228
PRIORITY APPLN. INFO.:			US 1994-366779	A 19941230
			US 1991-774475	B2 19911010
			US 1992-817919	B2 19920108
			US 1992-959952	B1 19921013
			US 1994-307382	A2 19940914
			WO 1995-IB1167	W 19951228
AB	Linoleic acid is converted into .gamma.-linolenic acid (GLA) by the enzyme .DELTA.6-desaturase . The present invention is directed to isolated nucleic acids comprising the .DELTA.6-desaturase gene. More particularly, the isolated nucleic acid comprises the promoter, coding region and termination regions of the .DELTA.6-desaturase gene. The present invention provides recombinant constructions comprising the .DELTA.6-desaturase coding region in functional combination with heterologous regulatory sequences. The nucleic acids and recombinant constructions of the instant invention are useful in the prodn. of GLA in transgenic organisms.			

L7 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:418024 CAPLUS

DOCUMENT NUMBER: 125:80514

TITLE: A plant **.DELTA.6** palmitoyl-acyl carrier protein **desaturase** and a **cDNA** encoding it and their use in the manufacture of 6-hexadecenoic acid

INVENTOR(S): Cahoon, Edgar B.; Ohlrogee, John B.
 PATENT ASSIGNEE(S): Michigan State University, USA
 SOURCE: PCT Int. Appl., 34 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9613591	A2	19960509	WO 1995-US13784	19951025 <--
WO 9613591	A3	19960808		
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5654402	A	19970805	US 1994-329560	19941026 <--
US 5614400	A	19970325	US 1995-539798	19951005 <--
AU 9641961	A1	19960523	AU 1996-41961	19951025 <--
PRIORITY APPLN. INFO.:			US 1994-329560	19941026
			WO 1995-US13784	19951025

AB A **.DELTA.6** palmitoyl-acyl carrier protein **desaturase** of *Thunbergia alata* and a **cdna** encoding the **desaturase** are described. The **cdna** may be expressed in transgenic plants for biosynthesis of 6-hexadecenoic acid in glycerides for industrial or food use. The **desaturase** introduced a double bond at the sixth carbon atom from the carboxyl end of a 16 carbon satd. fatty acid, and is therefore useful in prodn. of plant seeds having a modified fatty acid profile. The **cdna** was cloned from a seed endosperm library by amplification with conserved sequence-derived primers and screening with the primary amplification products.

L7 ANSWER 6 OF 14 SCISEARCH COPYRIGHT 2002 ISI (R)
 ACCESSION NUMBER: 97:140595 SCISEARCH
 THE GENUINE ARTICLE: WG561
 TITLE: Molecular cloning of a gene (Tp9ds) encoding Delta 9 fatty acid **desaturase** and growth-associated changes in mRNA expression in *Tetrahymena pyriformis*
 AUTHOR: Zhao Y T; Nakashima S; Nozawa Y (Reprint)
 CORPORATE SOURCE: GIFU UNIV, SCH MED, DEPT BIOCHEM, TSUKASAMACHI 40, GIFU 500, JAPAN (Reprint); GIFU UNIV, SCH MED, DEPT BIOCHEM, GIFU 500, JAPAN
 COUNTRY OF AUTHOR: JAPAN
 SOURCE: EUROPEAN JOURNAL OF PROTISTOLOGY, (31 DEC 1996) Vol. 32, No. 4, pp. 539-544.
 Publisher: VCH PUBLISHERS INC, 303 NW 12TH AVE, DEERFIELD BEACH, FL 33442-1788.
 ISSN: 0932-4739.
 DOCUMENT TYPE: Article; Journal
 FILE SEGMENT: AGRI
 LANGUAGE: English
 REFERENCE COUNT: 30

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A gene encoding Delta(9) fatty acid **desaturase** (Tp9ds) was cloned from *Tetrahymena pyriformis* W **cdna** library. The open reading frame encoded a protein of 292 amino acid residues, which was highly homologous to Delta(9)-**desaturases** of *T. thermophila*, carp and rat. The deduced amino acid sequence has histidine cluster motifs (one HXXXXH, two HXXHH) and two hydrophobic regions which are conserved in Delta(9)-**desaturases** from other sources. The Tp9ds gene was

present as a single copy in the *T. pyriformis* W genome as inferred by Southern blot analysis. Our previous studies have shown that with increasing age of culture, *T. pyriformis* cells showed an increased membrane fluidity accompanied with an enhanced Delta(9)-**desaturase** activity at the exponential phase, and that its activity decreased at the stationary phase. However, the mechanism underlying changes in the **desaturase** activity has not fully been understood. In this study, the Tp9ds mRNA level was analyzed by Northern blotting at the different growth stages. There was a marked increase in Tp9ds mRNA level at the mid-post exponential phase, followed by a decrease thereafter. These results suggest that changes of Delta(9)-**desaturase** activity during cell growth are regulated at least in part at the transcriptional level in *T. pyriformis*.

L7 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2
 ACCESSION NUMBER: 1997:336764 CAPLUS
 DOCUMENT NUMBER: 127:14504
 TITLE: Genes for fatty acid **desaturases** and choline oxidase are responsible for tolerance to low-temperature and salinity stresses in cyanobacteria and plants
 AUTHOR(S): Murata, Norio; Wada, Hajime; Sakamoto, Toshio; Tasaka, Yasushi; Gombos, Zoltan; Moon, Byoung Yong; Deshniun, Patcharaporn; Los, Dmitry A.; Hayashi, Hidenori
 CORPORATE SOURCE: National Institute for Basic Biology, Okazaki, 444, Japan
 SOURCE: Physical Stresses in Plants: Genes and Their Products for Tolerance, Proceedings of the Workshop on Genes and Their Products for Tolerance to Physical Stresses in Plants, Maratea, Italy, Sept. 24-27, 1995 (1996), Meeting Date 1995, 55-63. Editor(s): Grillo, Stefania; Leone, Antonella. Springer: Berlin, Germany.
 CODEN: 64JRAU
 DOCUMENT TYPE: Conference; General Review
 LANGUAGE: English
 AB A review with 26 refs. Most cyanobacteria and plants contain high levels of polyunsatd. fatty acids of membrane lipids. The authors have isolated the desA, desB and desC genes of *Synechocystis* sp. PCC 6803 which encode the .DELTA.12, .DELTA.15 (.omega.3) and .DELTA.9 **desaturases**, resp., of the acyl-lipid type. They disrupted the desA gene and the desD gene (for .DELTA.6 **desaturase**) in *Synechocystis* sp. PCC 6803 by insertion of antibiotic resistance gene cartridges. These mutations greatly modified the extent of unsatn. of the fatty acids of membrane lipids. These changes in the unsatn. of membrane lipids altered the tolerance of cyanobacterial cells to low temp. In higher plants, the authors isolated a cDNA for acyl-ACP:glycerol-3-phosphate acyltransferase from squash and introduced it into tobacco plants. The transformation modified the level of unsatn. of chloroplastic phosphatidylglycerol, and altered the tolerance of tobacco plants to low temp. Glycinebetaine, a compatible solute, is synthesized in some halophilic plants. From the soil bacterium *Arthrobacter globiformis*, the codA gene for choline oxidase, which converts choline into glycine betaine, was cloned. When this gene was introduced into *Synechococcus* sp. PCC 7942, the resultant transformants accumulated glycine betaine to some extent and became tolerant to salinity stresses.

L7 ANSWER 8 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3
 ACCESSION NUMBER: 1995:29988 BIOSIS
 DOCUMENT NUMBER: PREV199598044288
 TITLE: DELTA-6Hexadecenoic acid is synthesized by the activity of a soluble **DELTA-6** palmitoyl-acyl

carrier protein **desaturase** in *Thunbergia alata* endosperm.

AUTHOR(S): Cahoon, Edgar G. (1); Cramner, Ann M.; Shanklin, John; Ohlrogge, John B.

CORPORATE SOURCE: (1) Biol. Dep., Building 463, Brookhaven National Lab., Upton, NY 11973 USA

SOURCE: Journal of Biological Chemistry, (1994) Vol. 269, No. 44, pp. 27519-27526.
ISSN: 0021-9258.

DOCUMENT TYPE: Article

LANGUAGE: English

AB D-6 Hexadecanoic acid (16:1-**DELTA-6**) composes more than 80% of the seed oil of *Thunbergia alata*. Studies were conducted to determine the biosynthetic origin of the double bond of this unusual fatty acid. Assays of fractions of developing *T. alata* seed endosperm with (1-14C)palmitoyl (16:0)-acyl carrier protein (ACP) revealed the presence of a soluble **DELTA-6 desaturase** activity. This activity was greatest when 16:0-ACP was provided as a substrate, whereas no desaturation of the coenzyme A ester of this fatty acid was detected. In addition, **DELTA-6:0-ACP desaturase** activity in *T. alata* endosperm extracts was dependent on the presence of ferredoxin and molecular oxygen and was stimulated by catalase. To further characterize this enzyme, a **cdna** encoding a diverged acyl-ACP **desaturase** was isolated from a *T. alata* endosperm **cdna** library using polymerase chain reaction with degenerate oligonucleotides corresponding to conserved amino acid sequences in **DELTA-9stearoyl (18:0)- and DELTA-416:0-ACP desaturases**. The primary structure of the mature peptide encoded by this **cdna** shares 66% identity with the mature castor **DELTA-918:0-ACP desaturase** and 57% identity with the mature coriander **DELTA-416:0-ACP desaturase**. Extracts of *Escherichia coli* that express the *T. alata* **cdna** catalyzed the **DELTA-6** desaturation of 16:0-ACP. These results demonstrate that 16:1-**DELTA-6** in *T. alata* endosperm is formed by the activity of a soluble **DELTA-6:0-ACP desaturase** that is structurally related to the **DELTA-918:0- and DELTA-416:0-ACP desaturases**. Implications of this work to an understanding of active site structures of acyl-ACP **desaturases** are discussed.

L7 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1993:464918 CAPLUS

DOCUMENT NUMBER: 119:64918

TITLE: **.DELTA.-6-desaturase** of *Synechocystis*, and cloning and expression of its gene for manufacture of **.gamma.-linolenic acid**

INVENTOR(S): Thomas, Terry; Reddy, Avutu S.; Nuccio, Michael; Freyssinet, Georges

PATENT ASSIGNEE(S): Rhone-Poulenc Agrochimie, Fr.

SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9306712	A1	19930415	WO 1992-US8746	19921013 <--
W: AU, BG, BR, CA, CS, HU, JP, KR, PL, RO, RU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
ZA 9207777	A	19930421	ZA 1992-7777	19921009 <--
IL 103407	A1	19990922	IL 1992-103407	19921009
CN 1072722	A	19930602	CN 1992-113085	19921010 <--
CN 1053469	B	20000614		
AU 9228812	A1	19930503	AU 1992-28812	19921013 <--

AU 667848	B2	19960418		
BR 9206613	A	19950411	BR 1992-6613	19921013 <--
JP 07503605	T2	19950420	JP 1992-507243	19921013 <--
EP 666918	A1	19950816	EP 1992-922205	19921013 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, SE				
HU 69781	A2	19950928	HU 1994-1007	19921013 <--
HU 217328	B	19991228		
RO 113256	B1	19980529	RO 1994-585	19921013
CZ 285471	B6	19990811	CZ 1994-817	19921013
RU 2152996	C2	20000720	RU 1994-30816	19921013
CN 1174236	A	19980225	CN 1997-104566	19970321

PRIORITY APPLN. INFO.:

US 1991-774475	A	19911010
US 1992-817919	A2	19920108
WO 1992-US8746	A	19921013

AB The gene for **.DELTA.-6-desaturase** (I) of *Synechocystis* is cloned, sequenced, and expressed for manuf. of **.gamma.-linolenic acid** (II). The I gene was cloned from a partially *Sau3A*-restricted genomic library of *Synechocystis* (PCC 6803) by the gain-of-function method using a filamentous cyanobacterium *Anabaena* deficient in II but rich in linoleic acid. Also cloned was **.DELTA.-12-desaturase** (III) gene using an oligonucleotide probe derived from known III gene sequence. Expression of the I and III genes in *Synechococcus* (PCC 7942) deficient in linoleic and II was shown. The recombinant *Synechococcus* produced II from oleic acid. Also shown was the expression of I gene in tobacco plant.

L7 ANSWER 10 OF 14 MEDLINE

ACCESSION NUMBER: 93356506 MEDLINE
DOCUMENT NUMBER: 93356506 PubMed ID: 8394680
TITLE: Metabolism of radiolabelled 18:2n-6 and 18:3n-6 by NIH-3T3 cells and the DT subclone.
AUTHOR: De Antueno R J; Cantrill R C; Ells G W; Elliot M; Huang Y S; Horrobin D F
CORPORATE SOURCE: EFAMOL Research Institute, Kentville, Nova Scotia, Canada.
SOURCE: ANTICANCER RESEARCH, (1993 Jul-Aug) 13 (4) 973-7.
Journal code: 8102988. ISSN: 0250-7005.
PUB. COUNTRY: Greece
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199309
ENTRY DATE: Entered STN: 19931001
Last Updated on STN: 19980206
Entered Medline: 19930914

AB The incorporation and metabolism of **delta-6-desaturase** substrate and product, [1-14C]-linoleic (18:2n-6) and [1-14C]-gamma-linolenic acid (18:3n-6), was examined in NIH-3T3 cells and the DT subclone which differs only in the presence of the v-Ki-ras oncogene. Similar amounts of post **delta-6** and **delta-5 desaturase** metabolites were found in both cell lines indicating that the activity of these important enzymes of fatty acid metabolism was not affected by the expression of the oncogene. However, measurable quantities of the direct elongation product of 18:2n-6, 20:2n-6, were only found in DT cells. Radiolabel was recovered predominantly from the phospholipid fraction at low fatty acid concentrations, whereas neutral lipid labelling occurred when higher concentrations of exogenous fatty acid were present. This effect was most pronounced in DT cells and may result from the presence of the activated ras oncogene.

L7 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1993:554815 CAPLUS
DOCUMENT NUMBER: 119:154815
TITLE: Isolation of a **.DELTA.6-desaturase** gene from the cyanobacterium

Synechocystis sp. strain PCC 6803 by gain-of-function expression in Anabaena sp. strain PCC 7120

AUTHOR(S): Reddy, Avutu S.; Nuccio, Michael L.; Gross, Lisa M.; Thomas, Terry L.

CORPORATE SOURCE: Dep. Biol., Texas A and M Univ., College Station, TX, 77843, USA

SOURCE: Plant Molecular Biology (1993), 22(2), 293-300
CODEN: PMBIDB; ISSN: 0167-4412

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The enzyme **.DELTA.6-desaturase** is responsible for the conversion of linoleic acid (18:2) to .gamma.-linolenic acid (18:3.gamma.). A cyanobacterial gene encoding **.DELTA.6-desaturase** was cloned by expression of a Synechocystis genomic cosmid library in Anabaena, a cyanobacterium lacking **.DELTA.6-desaturase**. Expression of the Synechocystis **.DELTA.6-desaturase** gene in Anabaena resulted in the accumulation of .gamma.-linolenic acid (GLA) and octadecatetraenoic acid (18:4). The predicted 359 amino acid sequence of the Synechocystis **.DELTA.6-desaturase** shares limited, but significant, sequence similarity with two other reported **desaturases**. Anal. of three overlapping cosmids revealed a **.DELTA.12-desaturase** gene linked to the **.DELTA.6-desaturase** gene. Expression of Synechocystis **.DELTA.6-** and **.eta.12-desaturases** in Synechococcus, a cyanobacterium deficient in both **desaturases**, resulted in the prodn. of linoleic acid and .gamma.-linolenic acid.

L7 ANSWER 12 OF 14 CABA COPYRIGHT 2002 CABI

ACCESSION NUMBER: 92:118984 CABA

DOCUMENT NUMBER: 921631942

TITLE: Enzymes and genes of fatty acid modification and triacylglycerol biosynthesis

AUTHOR: Murphy, D. J.; Hills, M. J.; Bowra, S.; Fairbairn, D.; Richards, D.; Ross, J. H. E.; Slocombe, S. P.; Taylor, R. D.; Whitfield, H. V.

CORPORATE SOURCE: Cambridge Laboratory, John Innes Centre, Colney, Norwich, NR4 7UH, UK.

SOURCE: Annual report 1991, AFRC Institute of Plant Science Research, Cambridge Laboratory, John Innes Institute, Nitrogen Fixation Laboratory and Sainsbury Laboratory, (1992) pp. 9-11.
Publisher: Plant Science Research Ltd. & John Innes Institute. Norwich

PUB. COUNTRY: United Kingdom

DOCUMENT TYPE: Report; Company Publication

LANGUAGE: English

AB Six enzymes of fatty acid modification and triacylglycerol biosynthesis in rapeseed (Brassica napus) are being studied as part of a programme to produce transgenic oilseed crops with fatty acid composition designed for specific industrial uses. A **DELTA 9** stearyl ACP **desaturase** [acyl-acyl carrier protein **desaturase**] **cdna** was obtained and used to **clone** a genomic DNA from rapeseed. This **cdna** is being used as a probe to **clone** the **DELTA 6 desaturase** gene from various Umbelliferae species into oilseed rape to produce an oil high in petroselinic acid, a potential source of detergents and plastics. Other preliminary results on the location and characterization of the enzymes and their substrates are briefly outlined.

L7 ANSWER 13 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
4

ACCESSION NUMBER: 1992:258217 BIOSIS
DOCUMENT NUMBER: BA93:134542
TITLE: EFFECTS OF N-3 AND N-6 FATTY ACIDS ON TUMOR NECROSIS FACTOR
CYTOTOXICITY IN WEHI FIBROSARCOMA CELLS.
AUTHOR(S): BREKKE O-L; ESPEVIK T; BARDAL T; BJERVE K S
CORPORATE SOURCE: DEP. CLIN. CHEM., UNIV. HOSP., UNIV. TRONDHEIM, N-7006
TRONDHEIM, NORWAY.
SOURCE: LIPIDS, (1992) 27 (3), 161-168.
CODEN: LPDSAP. ISSN: 0024-4201.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB Modulation by fatty acids of the cytotoxic effect of recombinant tumor necrosis factor alpha (TNF) toward WEHI 164 mouse fibrosarcoma cells has been examined. Preincubating the highly TNF-sensitive WEHI clone 13 cells for 44 hr with 50 .mu.mol/L of 20:5n-3, 22:6n-3, 18:3n-6, 20:3n-6 or 20:4n-6 reduced cell survival 22 hr after challenge with TNF (40 ng/L) by 65%, 72%, 60%, 98% and 85%, respectively. In comparison, 18:3n-3, 18:2n-6 and 18:1n-9 had only negligible effects on TNF-induced toxicity. Different extent of fatty acid incorporation into cell total phospholipids or triglycerides could not explain the observed effects on TNF cytotoxicity, and the enhanced cytotoxicity could therefore not be explained merely by an increased unsaturation of the cell membranes. In addition to the fatty acid supplied, preincubation with 18:2n-6, 18:3n-6 or 18:3n-3 also enriched the cells with 20:2n-6, 20:3n-6 and 20:3n-3, respectively, most likely due to chain elongation. The results suggest that the WEHI cells have a low **.DELTA.6 desaturase** activity, and that n-6 and n-3 acids must have at least 3 or 4 double bonds, respectively to enhance TNF cytotoxicity in WEHI cells. Dexamethasone partly inhibited TNF-induced cytotoxicity, while cyclooxygenase, thromboxane synthetase or lipoxygenase inhibitors had no or negligible effects. The antioxidant butylated hydroxyanisole (BHA) completely inhibited TNF-induced cytotoxicity, while the structurally and functionally similar antioxidant butylated hydroxytoluene had no such effect, indicating that BHA does not block TNF cytotoxicity through its antioxidant effect. The results suggest that TNF cytotoxicity involves, directly or indirectly, metabolism of long-chain polyunsaturated fatty acids, and we speculate that fatty acid metabolites are involved.

L7 ANSWER 14 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
5

ACCESSION NUMBER: 1986:374739 BIOSIS
DOCUMENT NUMBER: BA82:69715
TITLE: METABOLISM AND INCORPORATION INTO GLYCEROLIPIDS OF
EXOGENOUS 18 3-N-3 AND 18 3-N-6 BY MDCK CELLS.
AUTHOR(S): LYNCH R D; LOCICERO J; SCHNEEBERGER E E
CORPORATE SOURCE: DEP. PATHOL., COX BUILD. 5, MASS. GENERAL HOSP., BOSTON,
MASS. 02114.
SOURCE: LIPIDS, (1986) 21 (7), 447-453.
CODEN: LPDSAP. ISSN: 0024-4201.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB The extent to which exogenous 18:3(n-3) and 18:3(n-6) were desaturated and elongated and the degree to which they and their derivatives altered the unsaturation index of cell glycerolipids were compared using clone 4 MDCK cells grown in lipid- and serum-free medium. Despite differences in the degree of unsaturation of the individual polyunsaturated fatty acids produced from 18:3(n-3) or 18:3(n-6), the unsaturation index of phospholipids increased similarly from 0.7 in control cells grown in serum- and lipid-free medium to ca. 1.6 in those supplemented with fatty acid. The added fatty acids had little effect on cell growth. The conversion of 18:3(n-6) to 20:3(n-6) and 20:4(n-6) was more rapid than that of 18:3(n-3) to 20:4(n-3) and 20:5(n-3). No significant quantities of 20:3(n-3) or 18:4(n-3) were noted. When both 18:3 isomers were supplied simultaneously, marked differences in the amounts of some species of n-3

and n-6 polyunsaturated fatty acids were observed. The presence of 18:3(n-6) and/or its derivatives suppressed levels of 20:4(n-3) and 20:5(n-3), perhaps through inhibition of the **.DELTA.6** and **.DELTA.5 desaturases** responsible for their synthesis from 18:3(n-3). Similarly, 18:3(n-3), and/or its longer more unsaturated derivatives, diminished the formation of 20:4(n-6) from 18:3(n-6). No marked effect on the products derived from elongation alone were observed.